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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/513,024	02/25/00	VILEN B	2879-64

HM12/0808

Angela Dallas-Pedretti Phd
Sheridan Ross PC
1560 Broadway Suite 1200
Denver CO 80202-5141

EXAMINER	
ROARK, J	
ART UNIT	**PAPER NUMBER**
1644	16

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/513,024	Applicant(s) VILEN ET AL.
	Examiner Jessica H. Roark	Art Unit 1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 May 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-6,9,10,12-14,18-22 and 30-33* is/are pending in the application.

4a) Of the above claim(s) *12-14,20 and 32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-6,9,10,18,19,21,22,30,31 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *15* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 5/11/01 (Paper No. 14), is acknowledged.
Claims 2-3, 7-8, 11, 15-17, 23-29 and 34-49 have been cancelled.
Claims 1, 4-6, 9-10, 12, 18-22, 30 and 33 have been amended.
Claims 1, 4-6, 9-10, 12-14, 18-22 and 30-33 are pending.

Claims 12-14, 20 and 32 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

Claims 1, 4-6, 9-10, 18-19, 21-22, 30-31 and 33 *are under consideration in the instant application.*

2. Applicant's provision of second copy of the IDSs filed 6/8/00 (Paper No. 3) and 6/19/00 (Paper No. 4) is acknowledged with appreciation.

3. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 5/11/01 (Paper No. 14).
The rejections of record can be found in the previous Office Action (Paper No.12).

It is noted that New Grounds of Rejection are set forth herein.

4. Applicant's cancellation of Claims 2-3, 7-8, 11 and 15-17 has obviated the previous objections and rejections with respect to Claims 2-3, 7-8, 11 and 15-17.

5. In view of Applicant's amendment limiting the claimed methods to an antibody to the extracellular domain of the transducer component, filed 5/11/01 (Paper No. 14); the previous rejection under 35 U.S.C. 112, first paragraph, as it would apply to the instant claims, has been obviated.

6. In view of Applicant's amendment limiting the claimed methods to an antibody to the extracellular domain of the transducer component, filed 5/11/01 (Paper No. 14); the previous rejection under 35 U.S.C. 112, first paragraph, written description, as it would apply to the instant claims, has been obviated.

7. Applicant's amendment to include the limitation of an antibody to the extracellular domain of the transducer component, filed 5/11/01 (Paper No. 14) has obviated:
the previous rejection of claims 1, 3-4, 7-8, 10, 15-16, 18 and 33 under 35 U.S.C. 102(b) as being anticipated by Cambier et al. (Proc. Natl. Acad. Sci. USA 1988 85:6493-6497);
the previous rejection of claims 1, 3-4, 7, 15-16, 18, 21 and 33 under 35 U.S.C. 102(b) as being anticipated by Vilen et al. (J. Immunol. 1996 159:231-243); and
the previous rejection of claims 1, 3-4, 7-8, 10, 15-16, 18-19, 21-22, and 33 under 35 U.S.C. 102(b) as being anticipated by Suzuki et al. (Int. Archs. Allergy Appl. Immunol. 1982, vol. 69:269-301).

8. Claims 1, 4-6, 10, 18 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Nakamura et al. (Int. J. Hematol. 1996 64:39-46, of record, see entire document).

Applicant's arguments, filed 5/11/01 (Paper No. 14) have been fully considered with respect to the instant claims, but have not been found convincing, essentially for the reasons of record.

As previously noted in Paper No. 12, Nakamura et al. teach a method to desensitize a B cell receptor (BcR) by contacting said receptor with a antibody to the transducer component (see entire document, (e.g., "Abstract"). In addition, Nakamura et al. teach that the antibody is a divalent antibody (i.e., anti-Igβ/CD79b, e.g., "Title"); that the extracellular binding component comprises IgD or IgM (e.g., Figure 2); and that the antibody is contacted with the receptor in an *in vitro* assay (e.g., "Methods").

Applicant argues that even though Nakamura et al. utilize an antibody to the same transducer component as in the instantly recited method, the antibody of Nakamura et al. nevertheless did not induce receptor desensitization. Applicant points to the last sentence of page 43 of Nakamura et al. for support for this argument. However, while Nakamura et al. do conclude there that "the current protocol of *in vitro* treatment with anti-CD79b mAb did not induce B lymphocyte unresponsiveness"; Nakamura et al. in the next experiment go on to show that in alternate culture systems the anti-CD79b (Igβ) antibody does indeed suppress an *in vitro* B cell response (e.g., see section 3.4). Further, Nakamura et al. in their "Discussion" on pages 43-45 clearly consider the anti-CD79b antibody to be an effective suppressant of B cell responsiveness.

Thus based upon the teachings of the Nakamura et al. reference taken as a whole, there does not appear to be a patentable distinction between the claimed and referenced methods. Nakamura et al. teach contacting a B cell antigen receptor with an antibody that binds to the extracellular domain of the transducer component, as recited in the instant methods. Nakamura et al. observe end results (suppression of antibody response and B lymphocyte differentiation) that would be downstream consequences of causing a dissociation of and/or inhibiting the association of the extracellular ligand binding component and the transducer component. Therefore, the claimed limitations would be inherent in the method of Nakamura et al., especially when the same receptor (BcR) and the same regulatory compounds (anti-Igβ/CD79b antibodies) are employed in that method.

The rejection is maintained in the absence of evidence clearly establishing a patentable distinction between the claimed and referenced methods.

9. Claims 1, 4-6, 9-10, 18-19, 21-22, 30-31 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ways et al. (US Pat. No. 6,103,713, of record) in view of Nakamura et al. (Int. J. Hematol. 1996 64:39-46, of record), and in further view of Vilen et al. (J. Immunol. 1996 159:231-243, of record).

Applicant's arguments have been fully considered, but have not been found convincing, essentially for the reasons of record.

Applicant traverses the rejection of record on the grounds that there is no motivation to combine the teachings of Ways et al with that of either Nakamura et al. or Vilen et al., in particular because Vilen et al. teaches that long-term B cell unresponsiveness is independent of the PKC activation which is blocked in the method of Ways et al.

As found more fully in Paper No. 12,

Ways et al. teach a method for treating autoimmune diseases, including SLE, associated with B cell activation by inhibiting PKC, a component of the signaling cascade that is downstream of the BcR (see entire document, especially claims 13 and 14, and column 8);

Vilen et al. teach and review details of the BcR signaling cascade and that the BcR can be desensitized by uncoupling the receptor from the signal transduction pathway (see entire document, especially the Discussion on pages 241-242); and

Nakamura et al. teach that antibodies to the BcR transducer components Igβ (also known as CD79b) and/or Igα (also known as CD79a) have potential for therapeutic application in any situation in which it is desirable to suppress humoral immunity (i.e., antibody production) in a patient (see entire document, especially last two paragraphs on page 45) and that antibodies to the transducer components (e.g., CD79b) would be particularly desirable for *in vivo* use (see both the "Introduction" and "discussion", especially page 40, 1st paragraph).

In response to Applicant's argument that there is no suggestion to combine the references, the Examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In the instant case, (as noted previously in Paper No. 12), the ordinary artisan at the time the invention was made would have been motivated to substitute the antibody of Nakamura et al. for the PKC inhibitor utilized in the methods of Ways et al. for treating autoimmune diseases associated with B cell activation, including SLE, because the ordinary artisan at the time the invention was made would have recognized that the antibody of Nakamura et al. that acted upstream (proximal to the BcR) in the signal transduction pathway would be more efficacious than an inhibitor of PKC in blocking B cell activation, and because Nakamura et al teach that antibodies to the transducer components (e.g., CD79b) would be particularly desirable for *in vivo* use. The teachings of Vilen et al. that long-term B cell unresponsiveness is independent of PKC activation provides further motivation to substitute the anti-transducer component antibody for the PKC inhibitor because, although Ways et al. teach that the PKC inhibitor does function in methods of treating autoimmune diseases such as SLE; based upon the teachings of Nakamura et al. and Vilen et al. the ordinary artisan would have expected that an antibody to the transducer component would be even more efficacious in that the antibody would provide long-term B cell unresponsiveness.

Ways et al., Nakamura et al. and Vilen et al. provide sufficient teachings that one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success in producing the claimed invention, even without knowledge of the detailed mechanism of action or a full characterization of the signaling cascade. Ways et al. teach a highly desirable endpoint as a functional consequence of inhibiting the BcR signaling cascade. That PKC acts downstream (distal to the BcR) in the BcR signaling cascade was well known in the art at the time the invention was made, as taught and reviewed by Vilen et al. Nakamura et al. teach the antibody to the extracellular domain of the transducer component of the BcR, and that antibodies to the transducer components would be particularly desirable for *in vivo* use in methods of suppressing humoral immunity, such as SLE.

Thus the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

The rejection is therefore maintained, essentially for the reasons of record.

10. No claim is allowed.

11. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica H. Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday, 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Jessica Roark, Ph.D.
Patent Examiner
Technology Center 1600
August 6, 2001

PHILLIP GAMBEL
PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
TECH CENTER 1600
8/7/01